I. Brief scientific abstract

A tumor nodule will be resected from a patient with advanced cancer and the lymphocytes (TIL) infiltrating into this cancer deposit will be cultured and expanded in vitro using techniques previously used in our adoptive immunotherapy protocols. When these TIL have reached log phase growth they will be incubated with a retroviral vector LTSN (containing genes for tumor necrosis factor and for neomycin resistance). These cells will then be expanded in culture until approximately 4×10^{10} cells are achieved. These TIL will then be cryopreserved in 10^{10} cell aliquots and tested to insure that they are free of replication competent virus and to determine the levels of tumor necrosis factor that are secreted. These gene-transduced TIL will then be administered to the cancer patient in escalating doses beginning at 10^{10} TIL along with 180,000 IU/kg of IL-2 every 8 hours for up to five days. Three weeks later the dose will be escalated to 3×10^{10} TIL and at three weekly intervals, escalated to 10^{11} and then to 3×10^{11} TIL. Extensive monitoring of patients will be performed to test for any toxic side effects resulting from the TIL administration. Studies of the survival and distribution of the gene-modified TIL will be performed by sequential sampling of blood, lymph nodes and tumor biopsy material. Tests for in vivo production of tumor necrosis factor will be conducted by measuring serum TNF levels and tests for the presence of the TNF gene and the NeoR gene will be performed by PCR-DNA analysis. Evaluation of the possible therapeutic response of cancer deposits to this therapy will be measured. The maximum dose of gene-transduced TIL that can be safely administered, will be determined in at least five patients. In subsequent patients transduced TIL will be selected in G418 and a similar escalating dose protocol will begin starting at 10% of the established safe number of unselected cells. When safe levels of non-selected and selected gene transduced TIL are determined, the dose of IL-2 will be raised to 720,000 IU/kg in a subsequent series of patients.